```
   1  ATRRYYLGAV ELSWDYMQSD LGELPVDARF PPRVPKSFPF NTSVVYKKTL
  51  FVEFTVHLFN IAKPRPPWMG LLGPTIQAEV YDTVVITLKN MASHPVSLHA
 101  VGVSYWKASE GAEYDDQTSQ REKEDDKVFP GGSHTYVWQV LKENGPMASD
 151  PLCLTYSYLS HVDLVKDLNS GLIGALLVCR EGSLAKEKTQ TLHKFILLFA
 201  VFDEGKSWHS ETKNSLMQDR DAASARAWPK MHTVNGYVNR SLPGLIGCHR
 251  KSVYWHVIGM GTTPEVHSIF LEGHTFLVRN HRQASLEISP ITFLTAQTLL
 301  MDLGQFLLFC HISSHQHDGM EAYVKVDSCP EEPQLRMKNN EEAEDYDDDL
 351  TDSEMDVVRF DDDNSPSFIQ IRSVAKKHPK TWVHYIAAEE EDWDYAPLVL
 401  APDDRSYKSQ YLNNGPQRIG RKYKKVRFMA YTDETFKTRE AIQHESGILG
 451  PLLYGEVGDT LLIIFKNQAS RPYNIYPHGI TDVRPLYSRR LPKGVKHLKD
 501  FPILPGEIFK YKWTVTVEDG PTKSDPRCLT RYYSSFVNME RDLASGLIGP
 551  LLICYKESVD QRGNQIMSDK RNVILFSVFD ENRSWYLTEN IQRFLPNPAG
 601  VQLEDPEFQA SNIMHSINGY VFDSLQLSVC LHEVAYWYIL SIGAQTDFLS
 651  VFFSGYTFKH KMVYEDTLTL FPFSGETVFM SMENPGLWIL GCHNSDFRNR
 701  GMTALLKVSS CDKNTGDYYE DSYEDISAYL LSKNNAIEPR SFSQNPPVLK
 751  RHQREITRTT LQSDQEEIDY DDTISVEMKK EDFDIYDEDE NQSPRSFQKK
 801  TRHYFIAAVE RLWDYGMSSS PHVLRNRAQS GSVPQFKKVV FQEFTDGSFT
 851  QPLYRGELNE HLGLLGPYIR AEVEDNIMVT FRNQASRPYS FYSSLISYEE
 901  DQRQGAEPRK NFVKPNETKT YFWKVQHHMA PTKDEFDCKA WAYFSDVDLE
 951  KDVHSGLIGP LLVCHTNTLN PAHGRQVTVQ EFALFFTIFD ETKSWYFTEN
1001  MERNCRAPCN IQMEDPTFKE NYRFHAINGY IMDTLPGLVM AQDQRIRWYL
1051  LSMGSNENIH SIHFSGHVFT VRKKEEYKMA LYNLYPGVFE TVEMLPSKAG
1101  IWRVECLIGE HLHAGMSTLF LVYSNKCQTP LGMASGHIRD FQITASGQYG
1151  QWAPKLARLH YSGSINAWST KEPFSWIKVD LLAPMIIHGI KTQGARQKFS
1201  SLYISQFIIM YSLDGKKWQT YRGNSTGTLM VFFGNVDSSG IKHNIFNPPI
1251  IARYIRLHPT HYSIRSTLRM ELMGCDLNSC SMPLGMESKA ISDAQITASS
1301  YFTNMFATWS PSKARLHLQG RSNAWRPQVN NPKEWLQVDF QKTMKVTGVT
1351  TQGVKSLLTS MYVKEFLISS SQDGHQWTLF FQNGKVKVFQ GNQDSFTPVV
1401  NSLDPPLLTR YLRIHPQSWV HQIALRMEVL GCEAQDLY
```

Fig._1

```
GGCAATGGAG CGTGAAGAAG GGCCCCAGGG CTGACCCCGG CAAACGTGAC  (50)
CCGGGGCTCC GGGGTGACCC AGGCAAGCGT GGCCAAGGGG CCCGTGGGTG (100)
ACACAGGCAA CCCTGACAAA GGCCCCCCAG GAAAGACCCC CGGGGGGCAT (150)
CGGGGGGGTG TTGGCGGGTC ATGGGGGGGG CGGGTCATGC CGCGCATTCC (200)
TGGAAAAAGT GGAGGGGGCG TGGCCTTCCC CCCGCGGCCC CCTAGCCCCC (250)
CCGCAGAGAG CGGCGCAACG GCGGGCGAGC GGCGGGGGGT CGGGGTCCGC (300)
GGGCTCCGGG GGCTGCGGGC GGTGGATGGC GGCTGGCGTT CCGGGGATCG (350)
GGGGGGGGTC GGGGGGCGCT GCGCGGGCGC AGCCATGCGT GACCGTGATG (400)
AG                                                     (402)
```

Fig._2

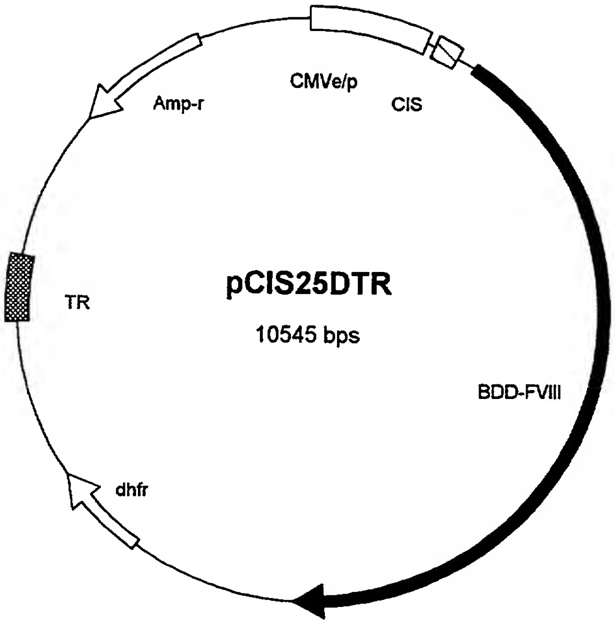


Fig._3

Fig._4A

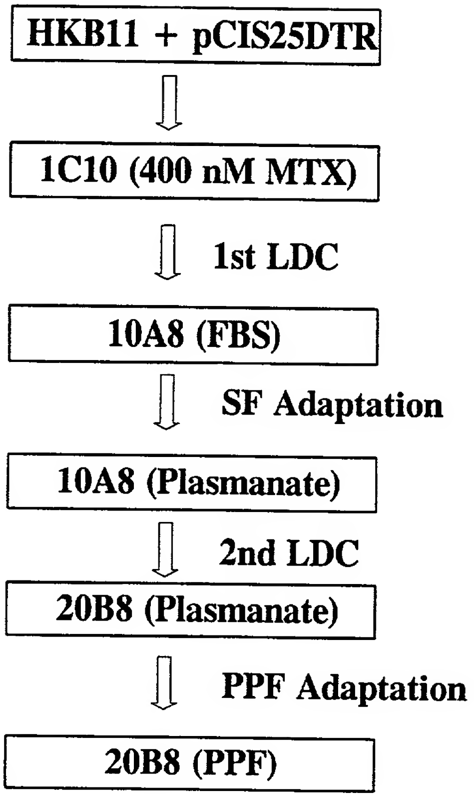
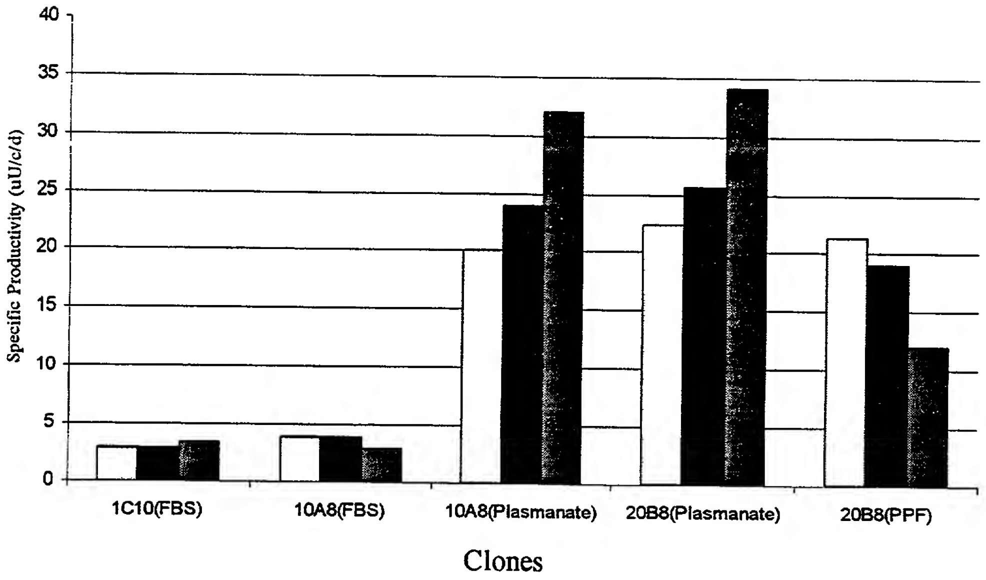

HKB11 + pCIS25DTR
1C10 (400 nM MTX)
1st LDC
10A8 (FBS)
SF Adaptation
10A8 (Plasmanate)
2nd LDC
20B8 (Plasmanate)
PPF Adaptation
20B8 (PPF)

Fig._4B


Specific Productivity (uU/c/d)
40
35
30
25
20
15
10
5
0
1C10(FBS)
10A8(FBS)
10A8(Plasmanate)
20B8(Plasmanate)
20B8(PPF)
Clones

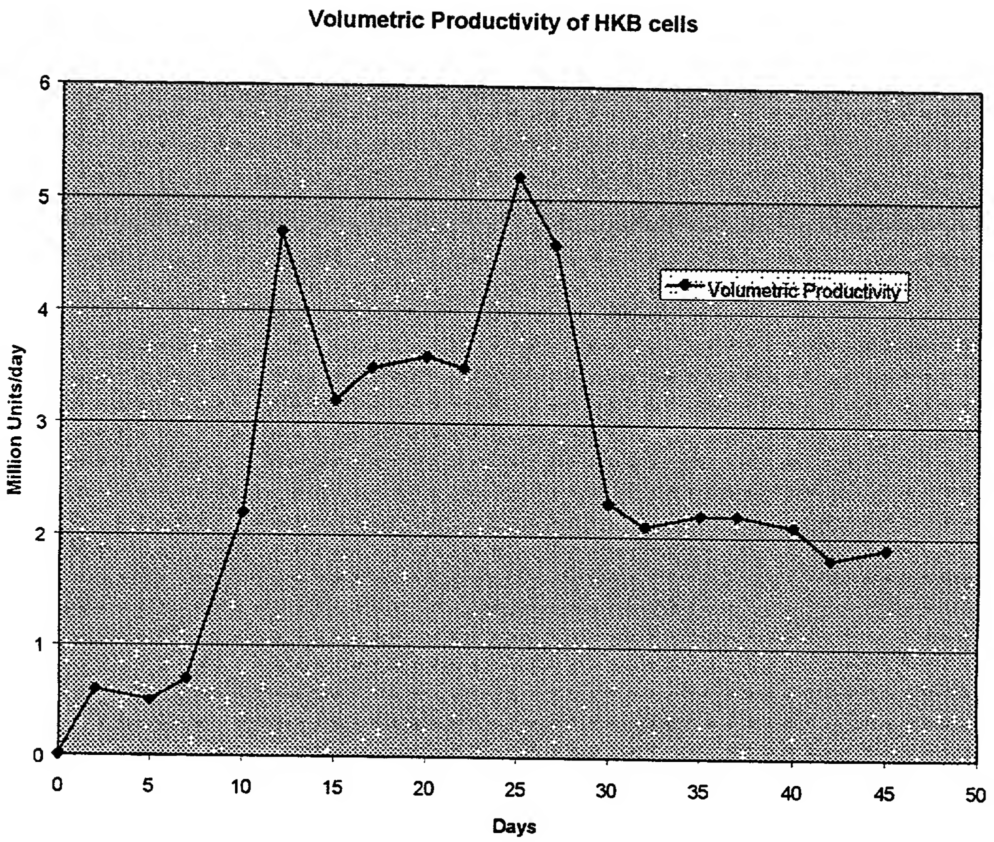

Volumetric Productivity of HKB cells
6
5
4
3
2
1
0
Million Units/day
0
5
10
15
20
25
30
35
40
45
50
Days
Volumetric Productivity

Fig._5